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ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE

DISEASES OF INFANTS AND CHILDREN

JOHN FITCH LANDON, M.D., Editor

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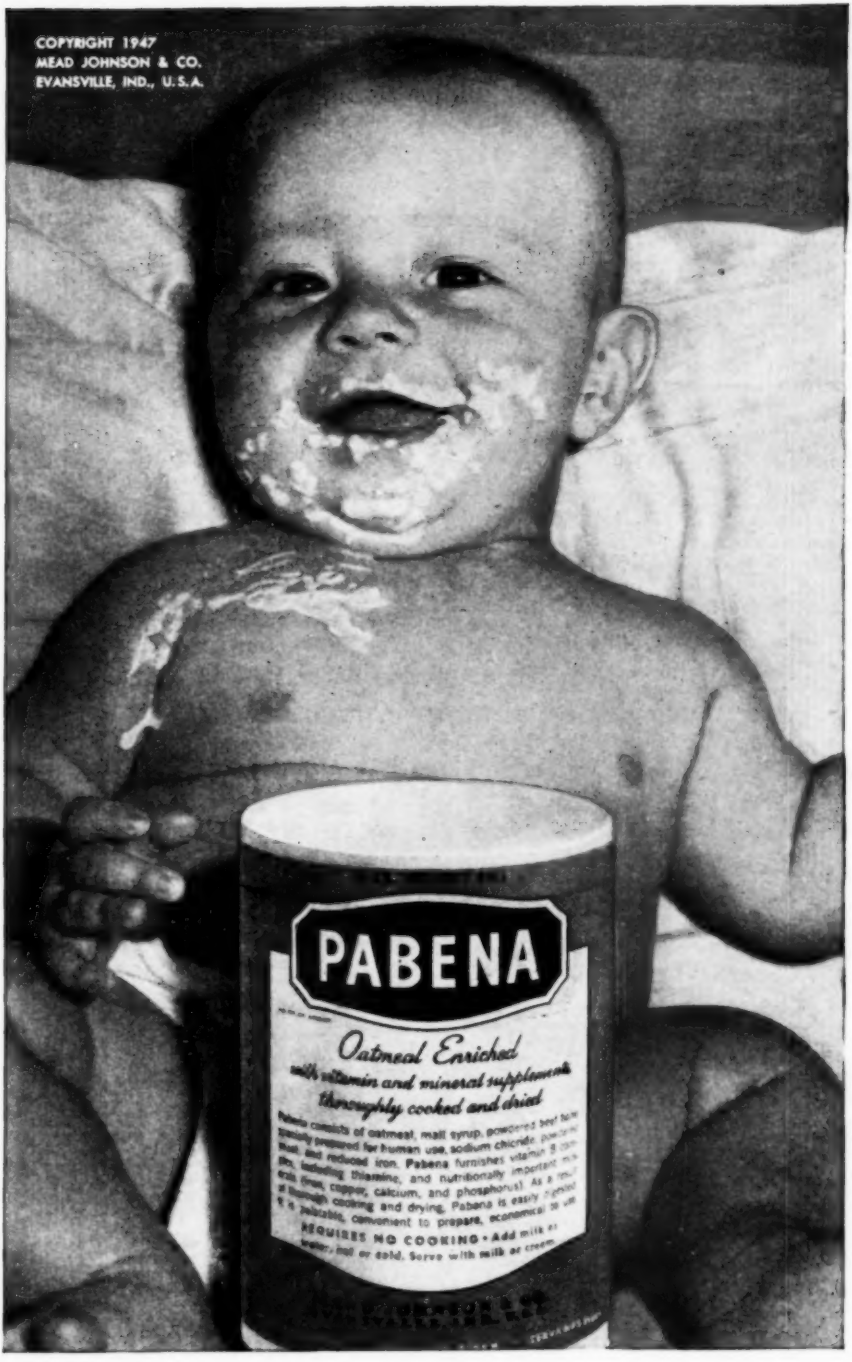
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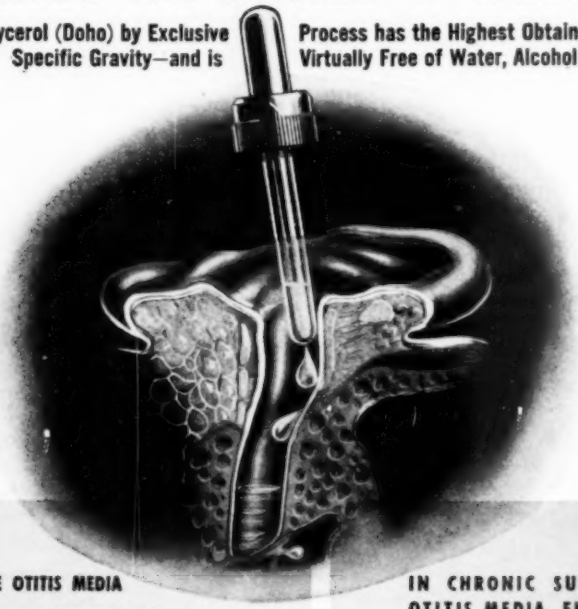

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ASTROBLASTOMA OF THE CEREBELLUM IN AN INFANT*

REPORT OF CASE

BRUCE F. GROTTS, M.D.
Wilmette, Ill.

Astroblastomas are rare in childhood, and only isolated cases have appeared in the literature. According to Bailey, Buchanan and Bucy[1] the most frequent tumor types in childhood are the astrocytoma (32 per cent), medulloblastoma (13 per cent), polar spongioblastoma (8 per cent), ependymoblastoma (7 per cent), and glioblastoma multiforme (7 per cent). Leavitt[2] believes that the glial tumors form the most important group in the preadolescent period.

Among the various reports of intracranial tumors in children, Globus, Zucher and Rubinstein[3] found no astroblastomas in 92 cases, and Stern[4], upon reviewing 102 cases, did not find any. Davis[5] reported 153 cases in children without finding an astroblastoma, while Rand and VanWagener[6] had a series of 38 without recording any tumor of that cell-type.

In Gross' series[7] of 9 cases, one was an astroblastoma of the cerebrum in a twenty-month-old child, and Sachs[8], in analyzing a series of 254 gliomas reported by Bailey and Cushing, found only 13 astroblastomas. In a larger series, Bailey and Bucy[9] reported 25 astroblastomas, but the youngest child was six years of age, and in Cushing's series[10] of 1,108 tumors, only 13 cases were astroblas-

*From the Milwaukee Children's Hospital.

tomas, the youngest patient being fifteen years of age. Later, in 1932, he discussed a total of 35 astroblastomas, none, however, being present in an infant.[11]

Gohier-Desplas and Dolto[12], in 1939, reported a single case of an astroblasto-astrocytoma in a child 3½ years of age, and Merwath[13] reported an astroblastoma in a 2½-year-old male child. This was approximately the age of the two patients reported by Bailey, Buchanan and Bucy (4 years and 3 years[1]).

In 1937, during the proceedings of the Association for Research in Nervous and Mental Diseases[14], thirteen astroblastomas were reviewed, and the youngest patients recorded were 2½ years and 14½ months. The former was a midline tumor, and the latter arose from the floor of the fourth ventricle.

The latter case, Gross' twenty-month-old case[7], and the one I am reporting, appear to be among the youngest on record.

CASE REPORT

M. W., a thirteen-month-old male, was admitted on May 3, 1948 to the Milwaukee Children's Hospital. The child was full term, had a normal birth, and had weighed eight pounds two ounces. He had received a regular diet and accessory foods, and had sat alone at ten months, but had not walked. The child had been well except for frequent colds, and had received the usual immunizations.

The mother was 33 years old and had been pregnant three times. One child was 2½ years of age, and was well except for a "kidney infection," and the other child was expected.

M. W. had seemed well until about one month before admission when he had begun to vomit. Vomiting was projectile and persistent, and occurred almost daily, usually just after feedings. It became progressively severe and the child lost weight. One week before admission he had a convulsion, but did not appear to lose consciousness. The convulsive movements appeared to be worse on the right side. He had five or six convulsions daily thereafter, and became increasingly restless. There was no crying during the week before admission, but only whining. Any handling of the infant seemed to precipitate an attack of "quivering" which would last three to five minutes. In the two weeks prior to admission he did not appear to be aware of his surroundings, and

his head seemed to become larger during the month prior to admission.

Dr. Neils Low admitted him to St. Mary's Hospital in Racine, Wisconsin, on April 30, 1948 where a spinal tap was done and roentgenograms were obtained. The x-ray of the skull revealed separated sutures and the xanthochromic spinal fluid contained 800 W.B.C. per cmm. and 140 mgm.% protein. A tentative diagnosis of brain tumor was made, and the child was referred to the Milwaukee Children's Hospital.

Examination on admission revealed a comatose infant with an expressionless face. All manipulations resulted in a whining-type cry. The head was markedly enlarged and the anterior fontanel was enlarged and tense. The pupils were equal and small and did not react to light or accommodation. The ocular muscles seemed normal. There was no nuchal rigidity, and the chest, heart and abdomen were normal. No testes could be felt in the scrotum. A mild clonic convulsion of all extremities was noted on stimulation. The left arm and leg seemed to have more tonus than the right, but the Kernig test was negative, and all other reflexes seemed equal and active. The Babinski test was positive on the left. The infant appeared to be in decerebrate rigidity.

Subdural taps were performed the day after admission, and the findings were normal. Ventricular punctures were done, and the fluid did not appear to be under any great increase of pressure. The fluid from the right lateral ventricle seemed more opalescent than the left, but the cell count was the same in both ventricles (less than 5 W.B.C. per cmm.), and the Pandy test revealed only a faint trace of globulin.

Ventriculograms were done the next day (May 5, 1948) and showed marked dilatation of both lateral ventricles without displacement. There was some dilatation of the third ventricle. No air was noted in the fourth ventricle, and the cranial sutures were separated. The thoracic and abdominal x-rays were normal. Radiologically, the impression was an infratentorial lesion with internal hydrocephalus.

On May 6, 1948, under local anesthesia, Dr. Harry Maxwell performed a right midline cerebellar craniotomy. When the dura mater was entered, an enormous grey, moderately vascular, soft, friable tumor mass was found in the midline. The deeper the dis-

section went, the firmer the tissue became. The cerebellar hemispheres were displaced laterally, and the tumor occupied the entire cerebellum directly over the fourth ventricle, extending up to the anterior cerebellar lobe. The entire mass was approximately the size of a tennis ball and extended downward into the herniated cerebellar tonsils. The gross tumor was entirely removed by suction and its point of origin was found to be along the cerebellar peduncles. The large remaining cavity was filled with saline and the wound was closed in layers, leaving the dura mater open over the right hemisphere.

Postoperatively, the child received 550 cc. of whole blood in divided doses and other intravenous fluids, parenteral vitamins and prophylactic penicillin.

Ventricular decompression taps were performed on several occasions with the removal of small amounts of bloody fluid under increased pressure. The child ran a febrile course between 102° and 103° F., and was unable to swallow well. On the eighth postoperative day he began to pass tarry stools, but otherwise the condition remained as before operation. He still presented the picture of decerebrate rigidity, could not swallow, and was fed by vein or gavage. The child's condition grew progressivly worse and he died on June 21, 1948, about six weeks after operation. Autopsy permission was not granted.

Laboratory: The urine showed one plus albumin and an occaisonal W.B.C. The blood count on admission revealed 11,200 leukocytes per cmm. with 57 per cent neutrophils and 15 grams of hemoglobin per 100 cc. The Kline test was negative.

Grossly, the tumor specimen consisted of several pieces of pale soft tissue of irregular shape, up to 2.5 cm. in their greatest dimension. In some parts the tumor was translucent and gelatinous, in others there were small areas of yellow necrotic tissue.

Microscopically, some of the tumor cells were polyhedral and in groups, while others were elongated and arranged radially around the numerous blood vessels. A few small areas of necrosis and calcification were seen. Phosphotungstic acid hematoxylin stain revealed many glial fibers, especially about the blood vessels. Dr. Gorton Ritchie's impression was astroblastoma of the cerebellum. Dr. Walter H. Jaeschke of Madison, Wisconsin reviewed the slides and agreed that this was an astroblastoma.

COMMENTS

Intracranial neoplasms in children are situated under the tentorium in 47.2 per cent of the cases, according to Critchley[15]. Symptoms and signs are commonly masked because of the age and un-united cranial sutures[16, 17]. The symptoms vary, depending on the location of the tumor (cerebral or cerebellar), but preoperative symptoms are often of shorter duration in the cerebellar types[14].

The onset of symptoms and signs may be acute, or slow and progressive, and the spinal fluid findings are not constant. Often such bizarre clinical patterns are produced that the diagnosis is frequently overlooked[17].

Most of the lesions, however, are cerebellar in origin and many children have enlarging heads and possibly a positive Macewen's sign on percussion[10]. Disorders of equilibrium and visual disturbances may be difficult to elicit because of the very young age. Vomiting and an enlarging head are two of the most important symptom-sign combinations in these children, although convulsions, listlessness, somnolence, hypotonia and static tremors may be present[10, 17]. The children may appear well despite frequent vomiting. This symptom, however, may be such a prominent feature that it can be of localizing value. According to Cushing[10], a median tumor of the cerebellum is so common in preadolescence that a child with unexplained vomiting, enlarging head and periodic unsteadiness should have eye-ground studies every week or so. The finding of a choked disc should always indicate a brain tumor until proved otherwise[16].

Histologically, the astroblastoma is less differentiated than the astrocytoma, and the predominating cell is an astroblast, which is the transitional cell between the spongioblast and the astrocyte[8]. The tumor is usually not well encapsulated but grows and infiltrates fairly slowly. It may be almost as benign as the astrocytoma or as malignant as the glioblastoma multiforme[11]. Surgically, it is apt to be mistaken for a protoplasmic astrocytoma and may be partly cystic[11].

According to the recently proposed Mayo Clinic glioma classification, however, this tumor could be called a grade ii or grade iii astrocytoma, since this classification groups the astrocytoma, astroblastoma and glioblastoma multiforme and then grades them

as astrocytomas, i through iv, depending on the degree of anaplasia[18].

The typical cell has a single large expansion attached to a blood vessel or connective tissue surface by a footplate. "In a hematoxylin and Van Gieson preparation the cell nuclei seem to draw away a certain distance from each blood vessel," and arrange themselves about it[14]. The elongated perivascular processes may be seen radiating from the blood vessels, and they may stain faintly with Mallory's phosphotungstic acid hematoxylin stain, silver carbonate or gold chloride[14]. A moderate degree of endothelial proliferation and a few mitotic figures may be present. Small nodules of calcification, sometimes in the vessel walls, but usually free in the tissue, often can be found[1, 14].

SUMMARY

1. An astroblastoma of the cerebellum in infancy is a rare tumor.

2. A case of an astroblastoma is reported in a 13-month-old infant.

3. Symptoms and signs are often masked because of the age and un-united cranial sutures.

4. The onset of symptoms may be slow or rapid.

5. The spinal fluid findings are not constant, but there may be a greatly increased protein content.

6. Vomiting, convulsions or somnolence, an enlarging head, and papilledema are characteristic of a brain tumor in infancy.

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CAUSES AND SYMPTOMS OF DYSLEXIA*

(Reading Difficulties)

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"We have a subnormal son, Henry, at home who can't learn to read," began the mother. But when the information was accumulated Henry proved to have normal intelligence.

"Everyone marvels at how ingenious our daughter, Betty, is in everything but she is not able to learn to read and she is so unhappy," reported another mother.

Such expressions of despair must challenge all groups concerned with the field of eugenics and allied subjects; particularly in child welfare and most intimately in the education which is so essential to good citizenship. But you ask, "What causes such a peculiar mental quirk?" It cannot be said with any degree of certainty what the causative factors are until an investigation is made of the child from every aspect. Thus is determined the influence on the mental processes of every experience to which the child has been exposed—physical illness, emotional disturbances, school adjustment, and so forth.

Dyslexia is a syndrome characterized by an inability to learn to read properly even though the individual's intelligence may be normal, or even superior. Dyslexia is the resultant of all abnormal factors which interfere with learning to read. These factors are *functional*, observable, preventable and correctable, in contradistinction to alexia. This dysfunction is comparable to that observed in other fields, such as dyspepsia, dysphagia, dysphonia or dysmenorrhea.

Ideas and learning are basically the reactions to perceptual experiences arising from sensations. These impressions cause the entire individual to react according to his intelligence and ability to interpret his past perceptual experiences. By these experiences he is enabled to arrive at an understandable concept, not only of his environment but also of his own introspective responses to contingencies with the resultant that he reacts directly to his psychobiologic needs. However, it is the complexity of these two aspects,

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i.e., inciting and responding by the recipient which reveals the great problem in interpretation of any situation, be it a distinct field of geometrical figures, a part of a field, or a sign or a symbol.

Generally the more intelligent a person is and the more perceptual experiences he has encountered, the more quickly he learns from symbols. Since printed letters and words are abstract symbols it is necessary to have had visual experiences in order to interpret their meanings when arranged in logical phrases. The entire central perceptual and conceptual processes are influenced by any stimuli which are present whether normal or abnormal, but the degree to which abnormal functions influence the process of learning depends upon the ability of the individuals to adapt themselves to the psychophysiologic needs or stimuli that exist at any particular time. The influence upon reading of this homeostatic[1] stability and adaptation depends on the relative degree of normality of all diverse activities which are synthesized into the reading processes.

INCIDENCE OF DYSLEXIA

According to the latest authoritative sources, from 15 to 25 per cent of the school population has some degree of dyslexia. This varies considerably with the standards of the school and the facilities of the home which are available to the child. However, dyslexia shows no preference for any particular social stratum.

Of the approximately two million children who leave their homes every fall to enter the first grade, between two hundred and fifty thousand and three hundred thousand will fail to pass at the end of the year, due to lack of reading skill. This naturally is cause for criticism of and comment on the educational progress by other people, and the child suffers the first severe defeat of his school life. As reading skill is usually the determinant for promotion this reaches alarming proportions when one realized that a "failure" in just one field soon spreads to "failure" in every field.

Some schools pass the unskilled into the next grade even though they are unable to qualify for such promotion. This policy warrants a careful review. But possibly nothing will be done about it until the school administrators and parents are willing to abandon the assumption that the teachers are to blame for the child's failure, although teachers can not escape their responsibility. As

soon as dyslexia is discovered, especially if it continues for an extended period, a concerted effort should be made to establish a remedial program, following a complete examination and determination of the causative factors.

The philosophy of promoting an incompetent child to avoid his realization of defect and subsequently the inferiority complex is perhaps understandable. But, to promote a mentally competent child from grade to grade even though he is unable to read is open to criticism. He should have the chance of having his difficulties corrected. As he is promoted from grade to grade under these circumstances, his difficulties become more pronounced until eventually he begins to show emotional disturbances, antisocial traits, etc. Peculiarly four times as many boys have dyslexia as girls. This has been the ratio in our series and it is hard to explain.

SOLUTION TO PROBLEM

It was with the purpose to help achieve a solution to this problem that the Dyslexia Memorial Institute was established in 1938. The staff is composed of an internist, a psychologist, a psychiatrist, an otolaryngologist, an ophthalmologist, educators and vocal teacher. After each staff member has examined the patient a conference is held at which time each examiner reports his findings and makes his recommendations for the treatment which he believes should be carried out. By grouping these recommendations a definite course of treatment is prescribed for each case individually. Once the plan of treatment has been established a conference is held with the parents at which time the findings are given. The children and parents are then instructed to return for weekly treatments and counseling as necessary, at which time the entire staff is present. This distinctly enhances the program. The child is expected to continue his ordinary school routine.

In order for the patient to be eligible for admittance into the Institute he is supposed to have an Intelligence Quotient (I.Q.) of 85 or better. This information must be furnished by the school or some other available source, otherwise the Institute's psychologist administers a preliminary test to determine if he is admissable. Even with this safeguard to avoid the "slow learning" type of child, we found in our series 24 cases with I.Q.'s ranging from

60 to 85. This cannot be overlooked and must be considered as an indictment against psychological reports made by individuals lacking the ability to administer and interpret psychological tests. Too often the child has been subjected to unjust criticism and pressure in trying to make his attainments equal his pseudomental abilities. The I.Q. may be much higher than reported and in turn this report may influence the parents and teacher to treat him as a mentally dull person; while actually many children are working above their mental age expectancy. In our series of 215 cases the highest full scale I.Q. was 147. The average I.Q. for our series, except for the 24 cases mentioned above, was 108. The average chronological age was 12 years 3 months. The youngest was 6 years 8 months and the oldest was 45 years of age. It was found advisable to give tests not only to determine vocabulary and verbal I.Q.'s but also their performance I.Q. before making recommendations. Many times there is a wide variation in these abilities.

PSYCHOLOGICAL IMPLICATIONS

From the psychological examination, it is important to note methods exhibited in work and play, especially methods of attacking a new problem, endurance, motor skills, fatigability and attitude. Also their reading vocabulary is estimated as to word form, word recognition and meaning of opposites. Furthermore, reading comprehension is determined according to ability to follow instructions and interpretations of printed material in story form.

In arithmetic both reasoning and fundamentals are considered in deciding their mathematical achievements, by solution of problems which include number sequence, money value and exchange, number and time, signs and symbols, addition, subtraction and multiplication of combinations.

The patients usually feel they are subnormal mentally because they are not learning as others in their class. Their personalities become warped not only because they feel that way, but because other people treat them as subnormals. Their sense of self reliance is lost and they may refuse to attempt even the simple tasks. Their sense of personal worth is low and the feeling of belonging may be affected adversely not only as to the school group but it may extend to the family itself. Thus they begin to withdraw from

social contacts and perhaps become day dreamers to live in a world of their own making. As pressure is exerted their sense of personal freedom diminishes and when they can find no solution to their dilemmas they begin to develop antisocial tendencies which eventually may lead to delinquency. This may not be ascertained merely by observing the conduct of the child but at times can be found as his emotions are projected during the tests of personality. Early recognition offers a better chance for correction than after a behavior problem has presented itself. Even though a child may have high social standards, as he rebels against regimentation his social skills become affected and others become critical of his conduct.

PSYCHIATRIC APPRAISAL

During the psychiatric appraisal one must study the characteristics of the patient and other occupants of the home, especially their hereditary traits and eccentricities of character and conduct; whether or not there is a broken home; family routine, especially meals and opportunity of child to discuss his problems with sympathetic parents; pressure exerted at home; comparison of the patient's achievements with those of other children: too high ideals by parents for the child's mental capabilities; overanxiety of parents with its detrimental effects; church affiliations; cooperation of the home with the school and with other social agencies. The patient's ability to adjust to usual normal behavior in clubs and social activities must be determined. Distraction in the home and elsewhere, such as too many movies or radio programs and the types permitted, should be found. It is essential to know the language usage in the home. The parents should be the "clearing house" for all orders pertaining to the child. The child should be responsible to them without too much interference from grandparents, aunts and uncles, or any other person. The parents should agree upon what standards are expected of the child, otherwise if one is a perfectionist the other may become too lax in discipline trying to compensate. Too many bosses should be avoided.

The psychiatric appraisal also determines the attitude of the child toward his failure, especially the reason for evasiveness in attacking the task at hand, or the reason for developing fear as expressed throughout the entire emotional and physical reactions.

Why the emotional block and frustration causing them to be resistant and to become indifferent? It is important to understand their conduct; whether domineering or whether use is made of some other means or situation to get and keep attention. Their alertness of observation of things and events should be noted. They may be lackadaisical or aggressive; harboring resentments toward any attempt at corrections. In general it is of vital importance to find some special interest by which to secure and keep sustained motivation.

EDUCATIONAL INFERENCE

In order to find the exact skill lacking in reading, it is necessary to study his early school life; age at which the child entered school, evidence of reading readiness at that time, methods of instruction used in teaching reading, particularly for the first two years, whether it was oral or non-oral or combined; number of absences during early school life from illnesses and in what grades they occurred. Notice must be taken of the time and under what circumstances the first failure occurred and the subsequent instructions received to help correct defects in reading and spelling. Each teacher's personality must be ascertained; whether she has a tendency to be a strict disciplinarian or to be too sympathetic.

Specifically one must find the grade level of the reading ability of the patient, observing the ease with which it is accomplished, noting reversals, insertions, omissions, substitutions, rate of reading, rhythm, comprehension and the ability to express ideas gotten from the subject matter. One must observe the kinesthetic responses to both oral and written requests, the recognition of the phonetic markings as a guide to their pronunciation, and the usage of punctuation marks. Compare silent reading efficiency, whether lip movement or not, with that of oral reading to ascertain whether some one is reading the required assignments to him. If some one is reading his assignments it would naturally eliminate any desire or incentive for the patient to read for himself. That is one way, of many, of keeping the child infantile with immature attitudes where he refuses to "grow up" and accept responsibilities not only in school but in his entire social and personal growth. One must determine the ability of word analysis, i.e., to break words into their component parts and also their aptitude in word building

Furthermore, a check must be made of practical everyday application of money values and exchange, weights and distances, etc.

PHYSICAL FACTORS

To find the physical influence as a causative factor a complete physical examination must be made.

In addition, special attention is made of the senses and equipment primarily concerned with dyslexia, such as auditory, vocal and ocular functions.

Preliminary to the physical examination a complete and detailed history from every aspect is necessary to aid in determinnig hereditary tendencies to constitutional dyscrasias, longevity, glandular imbalances; history of family diabetic tendencies, and tendency to tubercular diathesis; health of the mother during gestation; whether labor was normal or prolonged with complications; the early appetite and habits of feeding, whether breast or artificial or supplementary and at what age the biological functions were controlled. If enuresis persists, and many times it does, proper treatment should be instituted both through medication and proper emotional adjustment. Get a detailed account of the ontogenetic development, especially at what age he began to walk and talk. Another important detail should be the severity of acute or chronic illnesses which the child had during the preschool life and at what age and grade the child was absent from school due to these illnesses.

In the clinical laboratory a complete analysis should be made of the blood and urine to determine the exact metabolic functions of the individual. As glandular dysfunctions, especially of the thyroid, have been shown very definitely to influence learning, it is essential to have a determination of the basal metabolic rate. Evidence of malnutrition is noted by the lymphoid gland enlargements, abnormal weight and general appearance of the child. This general survey of the physical aspects of our problem has been attended to during the hospitalization period and during the periods of subsequent treatments.

HEARING AND VOICE

Hearing is an important factor in language function. At any time anything which interferes with hearing, in later life may bring about changes in personality, learning ability and reading.

As a result of partial deafness the child fails to come in normal contact with other children thereby causing a certain loss of learning opportunities as well as speech efficiency.

Acute otitis media is usually the cause of diminution of hearing. This may accompany measles, scarlet fever, or any other acute or chronic infection of the nose and throat as evidenced by hyperplasia and inflammation of the tonsils, adenoids, turbinates with stringy mucus over their surface or hypertrophied lymphatic nodules on the posterior pharyngeal wall.

Due to this hearing loss, the child may appear stubborn, inattentive, indifferent, "dumb" and eventually becomes an extreme introvert the more he withdraws from social contacts. It is essential that communications and directions given by parents and teachers to these children are heard and understood. They should be seated in the schoolroom to the best advantage.

To measure the ability of the individual to hear tones of different frequencies audiograms should be made in all cases. In addition the conversational and whispered voice should be used in testing, for occasionally there is a wide variation found in the comparison of these methods. Whether this variation is due to inattention or some other cause must be determined.

Nasal obstruction, sometimes allergies, frequently predisposes to reading disabilities. Sleep is interfered with, and as patients develop obstruction symptoms they assume not only the appearance of a low mentality but there is a possibility that the mentality itself is somewhat influenced.

Occasionally the upper part of the throat is not closed from the lower part of the nose and one has the "talking through the nose" twang, mostly due to a short palate—better leave the adenoids in if this is the reason. Sometimes the child has a long soft palate which he has difficulty in controlling. This is not surgical—better train the use of the voice, and teach him the enunciation of syllables, and how to control the soft palate. "Tongue tied" children are very infrequent but usually when a diagnosis has been made their difficulty is laryngeal. The aryepiglottic folds may be infantile.

Whereas vocalization is the phase through which most of our ideas and instructions are expressed, and since it is so closely related to the hearing, one must consider the physical development

and flexibility of the vocal organs and the patient's ability to coordinate and control them during the production of speech sounds. In order to have a well modulated voice one must cultivate the ability to have variation of utterances and durations of sound, which enables one to change the rate without cluttering the vocal sounds or stuttering and resulting in arrhythmia. The breathing posture must be learned, for upon this depends whether abnormal distribution of breath causes visable reactions as nervous twitchings. Faulty phonation as induced by tension or inhibitions which effect the vocal chords and laryngeal muscles result in breathlessness. This causes omissions, slurs and elision in which essential sounds are smothered beyond recognition or else entirely omitted; also substitutions may result. Malassimilation as a result of blending dissimilar sounds where words are rapidly pronounced is possible. In language usage one must study the faulty diction, mispronunciation, unconnected phrasing and misinterpretations, and ability to pronounce consonants and vowels at various positions in words. One must study the formation of the oral cavity and articulation of teeth, flexibility and positioning of the tongue and the use of lips and jaws in reading and speech.

VISUAL FUNCTION

If we accept the customary concept that reading is a simple reaction to visual stimuli, we would have to conclude that the visual process is the predominant factor in dyslexia. Almost invariably when mention is made of dyslexia to lay persons they preface the discussion with "that must be due to eye trouble." However, it is not as simple as that for it is necessary to consider abnormalities of the peripheral ocular mechanism as only a part of the symptom complex in retarded reading.

In our study[2] special attention was given to visual acuity, motility, fusion, stereopsis, ocular dominance, ductions for near and distance, recovering ability from diplopia during measurement of ductions, phorias both near and far, rate of reading, number of fixations and regressions calculated for 100 words, span of recognition, rhythm and coordination of eyes during reading and any other abnormalities which presented themselves.

Only nineteen per cent of the cases showed sufficient ametropia which required refraction. There were twice as many hyperopic

as myopic cases. Several spectacles were removed which had been prescribed empirically to aid the patient with his reading. Some of these patients had a high degree of exophoria which was aggravated by the convex lense.

No doubt, the excessive demand to attain clear vision upon the ocular neuromuscular mechanism results in fatigue which would lessen the incentive to learn, therefore, causing avoidance or neglect of reading.

Normal motility was present in ninety-three per cent of the cases.

Fusion ability was normal in ninety-seven per cent of the cases.

Extremely weak or no stereopsis were evident in twenty-two per cent of the cases. Only four per cent of these were due to tropias. The remaining learned stereopsis properly after training. Can this be another manifestation of dyslexia enigma?

In checking ocular dominance, eighty per cent of our cases showed no preference; eight per cent had a tendency to alternate; two per cent had a tendency to alternate but recovered quickly; two per cent had a tendency to suppress one eye and seven suppressed one eye completely.

The conclusions reached by other recent investigations dealing with the controversial questions of dominance, handedness, eyedness are somewhat conflicting. The evidence points to the conclusion that handedness is not significantly related to reading ability but that eye-hand dominance is probably present in some cases of reading disability.

Orthophoria was present in fifty-five per cent of the patients. Of the forty-five per cent which were heterphoric, half were exophoric for reading distance.

Weak fusion amplitude and weak recovery ability from diplopia during duction measurements are especially associated with dyslexia. With a low duction reserve coincident with convergent insufficiency or accompanying accommodative or convergent spasm, there is undue fatigue. This prevents the eyes from making efficiently the fusion responses and adjustments so necessary in getting and maintaining clear binocular vision, thereby causing blurring of the eyes or even temporary diplopia. This may be evidenced by some general physical or emotional disturbances.

Orthoptic treatments were recommended in fifty-two per cent of the cases.

In the overall picture of the peripheral ocular function, where rate of reading, number of fixations, regressions and span of recognition were considered, the dyslexia cases were inferior to that of the "norms."

Mirror reading or reversals are apparently self imposed psychological processes, maybe accidental at first, but with intrinsic significance, if analyzed in relation to current motivations and wishful aspirations of the child. His greatest desire is probably to get attention and have people comment on his rare condition. One of our cases could read upside down or backwards as well as he read when the book was held properly. We found no cases of typical mirror reading.

TREATMENT

The question is asked "What treatment is used in the correction of dyslexia?" The treatment depends on the diagnosis and ingenuity of the staff members, for there are no two cases which are identical, therefore, stereotyped methods are impractical. The primary goal should be to correct all abnormalities so the child will take over and do the work himself.

CONCLUSIONS

1. Dyslexia is a syndrome which is characterized by an inability to read properly even though the individual's intelligence is normal or even superior.

2. Every experience to which the child has been exposed influences the mental processes.

3. The degree to which abnormal stimuli influence the process of learning depends upon the ability of the individual to adapt himself to the psychophysiologic exigencies or needs that exist at any particular time.

4. The influence upon reading of this homeostatic stability and adaptation depends on the relative degree of normality of all diverse activities which are involved with the reading processes.

5. The incidence of dyslexia is sufficiently high and complex to require unanimity of all branches of medicine and other sciences in its solution.

6. For a diagnosis it requires a complete history from every aspect, physical and mental examinations, including intellectual and emotional appraisals; social investigations, educational achieve-

ments, including special abilities or disabilities and habits of work and play.

7. Psychological reports made by individuals lacking the ability to administer and interpret psychological tests should be ignored.

8. To promote an incompetent child to avoid his realization of defect is understandable but to promote a mentally competent child without giving him every opportunity of having his difficulties corrected is open to criticism.

9. Analysis of the specific reading difficulties, such as omissions, inserting and substitutions, for example, is helpful but only moderately so. It is important to find why these occur and to correct the basic causes.

10. History of early illness, malnutriiton, glandular imbalances and enuresis are concomitant to many cases.

11. Diminution of hearing may cause the child to appear stubborn, inattentive, indifferent, "dumb" and eventually he becomes an extreme introvert the more he withdraws from social contacts.

12. In order to have a well modulated voice one must have the ability to vary utterances and durations of sounds without suttering and resulting in arrhythmia. Faulty phonation may result in breathlessness which causes omissions, slurs and elision in which essential sounds are smothered beyond recognition or else entirely omitted; also substitutions may result.

13. The customary concept that reading is a simple reaction to visual stimuli must be modified. It is necessary to consider the ocular abnormalities as only a part of the symptom complex in retarded reading.

14. Mirror reading or reversals are apparently self imposed psychological processes, maybe accidental at first, but with intrinsic significance in relation to current motivations and wishful aspirations of the child to get attention or maybe used as a defense.

15. The method of treatment depends upon the diagnosis and ingenuity of the staff members. There are no two cases identical therefore streotyped methods are impractical.

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CLINICAL REVIEW

In order to encourage the writing of clinical articles by recent graduates or senior medical students, the ARCHIVES *will publish monthly at least one such paper from the classes of Doctor Reuel A. Benson, New York Medical College, New York; Doctor Philip Moen Stimson, Cornell Medical School, New York, and Doctor John A. Toomey, Western Reserve University Medical School, Cleveland. Other interested medical schools are cordially invited to submit student papers for consideration.*

ETIOLOGY OF RHEUMATIC FEVER*

PRESENT DAY CONCEPTS

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Introduction. Guillame de Baillou was the first to use the term rheumatism in 1642[1]. He used the term to describe acute polyarthritis as a separate disease and to distinguish satisfactorily acute rheumatism from gout. Over a hundred years elapsed before Bouilland emphasized the constant association of rheumatism and heart disease, and carefully demonstrated the frequent occurrence of endocarditis as well as pancarditis with rheumatism. Lecturing before the Harveian Society of London in 1888, Walter Butler Cheadle gave a classical description of the rheumatic state to which only a small amount of information can be added at the present time[1].

In the past forty years, research has centered on the bacteriological and immunological aspects of rheumatic fever in an unsuccessful attempt to determine the etiology. More recent studies, dealing with hypersensitivity, genetic and endocrine function, have allowed some light through the cloud which obscures this disease. These investigations are changing our concepts regarding the disease.

At present the literature is quite controversial. In the preparation of this material no attempt has been made to include a complete review of the many debatable aspects of rheumatic fever. Of necessity, only the more recent contributions from the voluminous literature are considered. The purpose of this paper is to present simply, and with a minimum of confusing data, concepts that seem

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currently to be most acceptable and most contributory to an understanding of the etiology of rheumatic fever.

Predisposing Factors. Present day statistics reveal that five times as many children die each year from rheumatic fever as from poliomyeletis, whooping cough, diphtheria, scarlet fever, measles and meningitis combined[116].

TABLE 1. *Predisposing Factors*

1. Sudden fluctuations of climate[3, 6, 38].
2. Poor housing[14, 56].
3. Crowded conditions[14, 56].
4. Inadequate diet and clothing[13, 29, 100].
5. Frequent respiratory infections[2, 3, 4, 25, 48].
6. Age[4, 31, 39].
7. Genetic factors[30, 31, 44].
   a. altered tissue immunity[13, 45, 52].
   b. hormonal imbalance[11].

In the United States the disease is reported to be less prevalent and milder in the southern states[4]. Observers have stressed the relative rarity of rheumatic fever in the tropical sectors of North, Central and South America[3,4]. The geographical distribution of rheumatic fever is unknown for the disease is endemic but uneven in its distribution. There is ample evidence to indicate that it is more common in urban areas in temperate climates throughout the world. Jones and his co-workers[3], in a discussion on the results of sending 26 rheumatic children from Boston to Florida, and in observations on the course of the disease in 40 rheumatic subjects living in Florida, found recurrences of activity in a large number of the subjects in both groups. In his preliminary observations of 88 rheumatic children, 6 to 16 years old, transported to Miami, Robinson[74] noted that the benefit derived from such a climate is "chiefly prophylactic." The increased incidence of rheumatic fever in the Rocky Mountain states necessitates further explanation, for the conditions under which these cases develop are not comparable to those in the New England states[14, 40]. Higbee[35] now considers climate to be relatively unimportant as a major factor in this disease.

It is difficult and of academic interest only to separate climate from geography as an epidemiological factor[30]. Rheumatic fever is far more prevalent in regions subject to cold, rain, and to sudden wide changes of temperature regardless of location[4, 67]. In accord with these facts are studies which consistently show the incidence

of this disease for the months of December to March to be the highest for the year[4, 15, 16].

Socio-economic conditions apparently play a considerable role as predisposing factors[100]. Although rheumatic fever is not limited to people in the lower income brackets, or to those who live in crowded areas, it seemingly is more frequent and severe in the poor. Unfavorable environmental surroundings, such as inferior housing, inadequate diet and clothing, and frequent respiratory infections, help account for the predominance of the disease among underprivileged children[2, 23].

One outstanding characteristic of rheumatic fever is the fact that the peak of incidence occurs during that period of life when the growth process is evolutionary and advancing [52, 88]. In a series of 696 subjects under observation by Wilson[4] from 1916-1935, the main age at the onset was 6.8 and 0.10 years, and about one year later for girls than for boys. The average age at onset as found by Ditkowsky[12] was 7.6 years. For practical purposes, we can consider the initial attack of rheumatic fever rare before the age of three and after forty[41]. The evidence is strongly suggestive that there may be some relation between rheumatic fever and the growth process. Coburn[53] also comments on the rarity of initial attacks in mature adults.

Sex does not appear to be an important factor as a predisposing cause[4]. Depending upon the series of cases reported, the incidence will be slightly higher in one sex[20]. When large numbers of patients are considered, the sex ratio is about equal. Thompson[42] felt that the disease is common in the redheaded, fair child with blue sclera, freckles or hyperextensible joints. Today this is of little value, for vulnerability to rheumatic fever does not appear to be influenced by physical characteristics. In the same light, there is as yet no conclusive evidence of a racial susceptibility to rheumatic fever[102, 103, 104].

The Streptococcus and the Post-streptococcic State. According to Wilson[4] rheumatic fever is probably an infection exhibiting a low degree of contagiousness in that not everyone exposed contracts the disease. Barnes[60] regards the disease as epidemic in type. Another opinion is that held by Lichtwitz[45] and others that rheumatic fever is a non-infectious disease. Despite this still raging conflict, it has become increasingly evident in the last thirty years that infection by hemolytic streptococci is, in some as yet

unexplained manner, related to the development of the rheumatic state. Of necessity, the evidence upon which this fact is based has been established in an indirect manner. Repeated attempts to isolate causative organisms which would satisfy Koch's postulates during all phases of the disease have met with failure.

The literature is rich with reports implicating the hemolytic streptococcus as the exciting factor of rheumatic fever[24, 67, 73]. Cohen[16] states that at present there is enough bacteriologic, serologic and epidemiologic evidence correlated with clinical experience to demonstrate the direct relationship of the streptococcus in the etiology of this disease. Classically, a history of an upper respiratory infection is usually present[68]. This infection may manifest itself as a pharyngitis, tonsillitis or "strep throat[36]." Streptococcal otitis media, sinusitis, scarlet fever or erysipelas may provoke acute rheumatic fever[25]. Kuttner and Reyersbach[48] are strongly convinced by their observations that the relationship between streptococcal pharyngitis and the reactivation of the rheumatic process is specific and securely establishes the importance of Lancefield Group A streptococci in the etiology of rheumatic fever. Coggeshall[37] recorded acute pharyngitis in 78 per cent of 266 patients who subsequently developed rheumatic fever.

An outbreak of an unusually large number of acute tonsillitis cases in a children's institution enabled investigators[12] to study the development of acute rheumatic fever. Of the 241 children who contracted streptococcic infection of the throat, 88, or 57 per cent, developed rheumatic fever. Numerous observers have confirmed this relationship between streptococcal tonsillitis and acute rheumatic fever; however, the question of tonsillectomy in preventing the onset of the disease is not settled. There is questionable evidence that preliminary tonsillectomy may modify the severity of juvenile rheumatism and in those whose tonsils are unhealthy after a first attack, tonsillectomy may be beneficial[56].

Investigations during the war years added greatly to our knowledge. When careful sampling of the throat cultures of new recruits revealed a high incidence of infection due to hemolytic streptococci, the prediction would be made that rheumatic fever would appear in the group in considerable incidence[27].

Previous studies have adequately demonstrated that rheumatic fever does not immediately follow an acute streptococcic infection, but is separated from it by a latent period of variable duration[34].

Coburn[52] has postulated three phases in the development of the disease:

Phase I. Streptococcal infection.
Phase II. Latent period of 1-3 weeks.
Phase III. Development of acute rheumatic fever.

Numerous papers based on intensive epidemiologic and bacteriologic studies confirm the presence of Phase I. Recrudescences of activity frequently appear when infection by hemolytic streptococci occurs in persons who have previously undergone attacks of rheumatic fever[26, 27]. Watson et al.[61] studied the complications and sequalae which occurred among 110 young adults with scarlet fever. Twenty-two developed unequivocal electrocardiographic abnormalities, three during their acute infection and nineteen later in post-scarlatinal convalescence. These abnormalities developed in 10 to 56 days during which time the patients were asymptomatic. The tracings were of the type commonly observed in patients with active rheumatic carditis. Such observations cause these investigators to consider it unreasonable to use a special name for the symtom complex of arthritis and carditis which follows scarlet fever from that applied to a very similar complex which may develop after pharyngitis or tonsillitis.

On the basis of this and other reports[64] the assumption can be made that rheumatic fever is a manifestation of the poststreptococcic state.

Dowd et al.[59] observed the reactions of rheumatic children to intradermal administration of scarlet fever toxin. An analysis of 275 reports submitted by 111 ambulatory rheumatic fever patients, 48 hours after an injection, revealed that not a single injection was followed by an attack of polyarthritis, carditis or chorea. According to these workers[28, 53], "the toxin has been used by us as a prophylactic measure against recurrence of acute rheumatic fever in children." Others have found that a high percentage of patients who had a rheumatic history developed joint pains following the injection of such a toxin[62, 63]. These results are interpreted as evidence that these individuals are sensitive to the erythrogenic toxin or perhaps other streptococcic products in the sterile filtrate injected. Young albino rabbits given a sterile erythrogenic filtrate of the NY-5 strain through daily subcutaneous injections over a considerable period of time showed many lesions typical of human

streptococcus disease and some cardiac lesions closely resembling those found in human rheumatic fever[55].

Wilson[4] reminds us that respiratory infections are responsible for the greatest morbidity in childhood and accompany many diseases other than rheumatic fever. A study[77] of the frequency of hemolytic streptococci in the throats of 756 well children revealed that there was no association between carrier rates and season, or between carrier rates and incidence of scarlet fever. Finally, it is a conceded fact that acute rheumatic fever can and does occur without a history of a previous streptococcic infection and after infection with other organisms[58, 75, 93].

The Latent Phase or the Allergic State. Many factors[43, 47, 68] point to the similarity of rheumatic fever pathogenesis and certain anaphylatic or allergic phenomena.[79, 82, 99] Assuming that the hemolytic streptococcus is the essential etiological agent, this would explain the failure to isolate the organism and the presence of a latent period. The fundamental reaction suggested[10] consists of a combination of a bacterial toxin with certain tissues of the host followed by an incubation or latent period and finally the explosive development of the clinical syndrome.[50] Apparently, this type of disease comes from a combining of body tissues with toxin to form an antigen. This is followed by a period during which antibodies against the tissue-toxin complex are elaborated; when there is a high enough titer, an autogenous antigen-antibody reaction occurs.[51, 59] The serum sickness type of reaction is a good example.[97]

Rich and Gregory[5, 6, 7] experimentally produced cardiac lesions having the basic characteristics of rheumatic carditis by subjecting rabbits to the intravenous administration of foreign protein. When horse serum was the agent used, cardiac lesions of the rheumatic type developed in 19 of 51 rabbits injected. No lesions were produced in six animals when streptococcal toxin was used. This stressed the importance of the individual host factor in determining the occurrence of rheumatic carditis-like lesions in sensitized animals. These investigators point out that focal hypersensitive lesions were produced in animals by circulating antigens that possess virtually no primary toxicity and are sufficiently similar to those of rheumatic carditis to provide a strong indication that human rheumatic lesions may represent the results of focal hypersensitive reactions to one or more soluble antigens.

Some evidence was found by Robinson[55] that normal horse serum injured the hearts of rabbits so that they became more susceptible to injury from a bacteria-free streptococcal filtrate. Alone, horse serum did not produce, in the 10 rabbits studied, a carditis like that observed by Rich and Gregory, a significant difference in the ability to form an injurious filtrate appeared among the various streptococci pathogenic for man. Inflammatory lesions more suggestive of an infection than an allergic etiology were produced with sterile NY-5 streptococcic filtrates. Robinson concludes that rheumatic fever is a special form of streptococcic injury dependent chiefly upon the peculiar host reactivity.

When rats are given injections of mixtures of killed streptococci and emulsions of specific rat tissues, such as heart, skeletal muscle and connective tissue, antibodies are produced which react in vitro with extracts of the tissue component used for immunization.[59] Since these antibodies cannot be produced by injections of the homologous tissue emulsions alone, that is, without streptococci, obviously the streptococci have the capacity to render certain substances of these tissues antigenic for the homologous species, presumably by some loose combination between streptococci and the tissue substances. The antibodies elaborated possess the ability to react with the tissue component alone. As a result of the pathogenic action of these auto-antibodies, changes chiefly affecting the valves and the other connective tissue structures of the heart which resemble those of rheumatic fever take place.[17] A recent report confirms the importance of auto-antibodies in glomerulonephritis.[107]

On the basis of these experimental results, Cavelti[17, 59] proposes the following hypothesis: During or succeeding the streptococcic infection which precedes a rheumatic attack by about two or three weeks, an autogenous antigen is formed by a reaction in which streptococcic substances or products combine with components of the susceptible host's tissues. This antigen stimulates the development of specific antibodies, which in turn precipitate the rheumatic lesions by reacting in vivo with the antigen situated in the tissues. Apparently once the formation of auto-antibodies has been incited, the streptococcic component is no longer necessary for the ensuing action of these antibodies on the tissues. Attempts to demonstrate in sera of acute rheumatic fever patients auto-antibodies to human heart were considered positive in 75

per cent of 67 patients tested according to Cavelti's collodion particle technique.

The experimental work is in general agreement with the clinical experiences of many observers.[57, 60] However, it is significant to mention that in some patients the latent period is not always present.[18, 57] Extensive analysis of rheumatic fever patients has led Rantz et al.[18, 49, 74] to assume that the disease is invariably induced by Group A hemolytic strepococci and that the clinical manifestations are the result of altered sensitivity of the tissues to some fraction or product of the organism. Numerous investigators have postulated the presence of an abnormal immune response in vulnerable individuals.

In brief, the latent phase in the development of acute rheumatic fever seems to be an allergic state. It appears to be the period of sensitization to the rheumatic antigen in the susceptible host. We must now turn our attention to the following questions: What is the rheumatic antigen? Can the susceptible host be defined?

The Rheumatic Antigen. The strains of hemolytic streptococci believed to be associated with the initiation of rheumatic fever belong to Lancefield's Group A. In vitro, several antigenic principles are produced: erythrogenic toxin, fibrinolysin, streptolysin S, streptolysin O, proteinase and hyaluronidase. A number of potential antigens are present within the bacterial cell, namely, nucleoproteins, type specific M substance and group-specific carbohydrate as well as others less well defined. Most patients in the rheumatic state, when Dick tested, react negatively indicating that neutralizing antibodies to the erythrogenic toxin are present. It is known that in scarlet fever the erythrogenic toxin can damage the endothelium of the vascular tree.[52]

Intensive research on the properties of streptococcal fibrinolysin[109] reveals that it is an enzyme. The name streptokinase has been offered to replace the present misnomer.[80] This bacterial enzyme acts upon serum protease and convefts it into a powerful lytic agent.[108] Antibodies which neutralize the enzyme activating property of streptokinase are termed antistreptokinases or antifibrinolysins. Quantitative antifibrinolysin estimations indicate that approximately 12 per cent of normal individuals have a high titer, that is, above 150 units. In only 29 per cent of patients with exudative tonsillitis from whom B-hemolytic streptococci were

cultured could a positive antifibrinolysin test be elicited. Antistreptolysin tests were positive, however, in 65 per cent of these patients.[69] Workers in this field caution that positive antifibrinolysin test in acute febrile diseases may be due to an antiprotease which prevents the action of the activated serum protease. Anderson and his co-workers[81] either prevented entirely or greatly decreased the expected antibody response to streptokinase by early and effective penicillin therapy which removed the infecting organism promptly from the nasopharynx. This is contrary to the results noted by Rantz et al.[80] who failed to observe any effect on antibody response by penicillin. Thus, a positive antifibrinolysin reaction, defined as an increase in the titer of two dilution increments, merely demonstrates a past infection by hemolytic streptococci. Rantz et al.[49, 80, 74] feel that it is becoming more apparent that the excessive formation of antibodies by individuals who develop manifestations of the post-streptococci state is the result of a non-specific immunologic hyperactivity. Guest et al.[103] report that antifibrinolysin activity is increased in a variety of acute and chronic medical illnesses.

Members of the Lancefield Group A elaborate two known streptolysins in vitro. Streptolysin S, a very toxic, unstable substance, is formed in the presence of serum and is responsible for the hemolysis of blood agar plates. At this time, no role in human disease has been attributed to this streptococcal product but it does stimulate the production of a neutralizing antibody in infected individuals which has been little investigated.

Streptolysin O is the heat and oxygen labile hemolysin that is produced in serum-free broth. This toxin has not been found to be etiologically responsible for any of the manifestations of streptococcal disease in man, but does incite the formation of an easily assayable antibody in infected human beings which has been extensively studied. Antistreptolysin O, the antibody, is associated with the gamma globulin fraction of the plasma proteins. The amount of this substance in the sera of healthy persons varies with the geographic area and age. Accordingly, a wide titer range has been observed in health thus rendering a single determination of the antistreptolysin level valueless. In one series the titer varied from patient to patient but the peak level was reached on the fourth week after onset of the acute illness in nearly all cases. Rantz et al.[74] clearly demonstrated that the mean production of

antistreptolysin was greater in patients selected by clinical criteria as examples of the rheumatic state than in those who recovered promptly from a streptococcic infection. These workers suggest that streptolysin may be the sensitizing antigen and that rheumatic fever arises in human beings who form excessive amounts of antistreptolysin following infection leading to "hypersensitivity of susceptible tissues."

The objections to such an hypothesis are many. Wilson et al.[72] concluded from their studies that the antistreptolysin titer in rheumatic children did not differ from that of non-rheumatic children. They did not find any significant correlation between the level of the titer and rheumatic activity. One should remember that the presence of a high antistreptolysin titer in a rheumatic patient does not denote rheumatic activity, and, similarly, a low titer does not signify quiescence. Taran, Jablon and Weyr[70] observed the antistreptolysin patterns of 460 rheumatic children and defined nine distinct patterns. An appreciable number of their patients presented the same patterns in their antistreptolysin titer when observed during any phase of active rheumatic disease. They conclude that the antistreptolysin curves determined in rheumatic children are expressions of the immunologic history of the individual; the antigen-antibody reaction of a person living in a streptococcal world. This antigen-antibody reaction may or may not be disturbed during the course of acute rheumatic disease.

Reitman[76] and others,[86] however, consider a rise in the antistreptolysin titer a diagnostic aid in carditis of obscure etiology. The estimation of the antistreptolysin level in patients is a more sensitive indicator of strepococcal disease than the antifibrinolysin test. It appears that this is due to a greater antigenicity of the streptolysin as compared to the fibrinolysin. A rising antistreptolysin titer is considered indicative of a streptococcal infection belonging to the Group A organisms.

The production of proteinase by hemolytic streptococci in various clinical conditions engaged the attention of Rothbard and Todd.[78] A correlation between the capacity of Group A streptococci to produce proteinase and the clinical reactions of patients to infection with these strains could not be made. In addition there appears to be no correlation between the occurrence of rheumatic fever and the antiprotease titer of the patient's serum.[33, 78]

Harris[66, 81] studied the various fractions of hemolytic streptococci by subjecting the organism to ultrasonic vibration and obtaining the products of bacterial disintegration. These fractions were: a residue(R), consisting of bacterial cell walls and the type-specific M protein; cytoplasmic particles(CP), containing lipoid, group specific carbohydrate and nucleoprotein of the ribose type; a supernatant portion (S) containing two components presumably protein. CP and S were able to precipitate and fix complement of antistreptococcic sera, produce antibodies and in general possessed a broad reactivity. Antibodies to these fractions were measured in the normal population and on the sera of patients with active and quiescent rheumatic fever. The serologic tests with CP and S substantiate the suggestion obtained from antifibrinolysin and antistreptolysin tests regarding the production of antibodies to streptococcal products in the rheumatic state. Anti-CP and anti-S titers continued at high levels long after the rheumatic process had reached quiescence. No relationship was found between the serologic titer of either antibody and the degree of clinical activity.

Recent studies indicate that the amount of inhibitory substance against streptococcal hyaluronidase in sera from patients with rheumatic fever is greater than in sera from patients early in the course of uncomplicated hemolytic streptococcic infections or from normal individuals.[83, 84] Early in the course of active rheumatic fever the serum antihyaluronidase titers have been found to be significantly higher than from any other group of patients studied.[85, 100] The relationship of streptococcal hyaluronidase to the pathogenesis of rheumatic fever cannot be evaluated at present.[83, 84, 85, 100]

It is a somewhat disheartening task to attempt to correlate this evidence. As long as these antigenic characteristics are ill understood, their antibody response will defy clarification. The concept that acute rheumatic fever may be considered a direct manifestation of the antigenic property of the hemolytic streptococcus can not be substantiated. Mote and Jones,[71] in an exhaustive immunologic study, failed to find any important difference between the rheumatic and non-rheumatic in the antibody response to products of the Group A streptococci. If the pathogenesis of rheumatic fever involves sensitization, the possibility that the sensitizing agent will not be detected is great because the degree of sensitization

and the titer of humoral antibodies to a given substance bear no necessary quantitative relationship to each other. The abnormal production of these antibodies may merely reflect an exaggerated immunologic hyperreactivity in individuals developing this disease. It is quite possible then, that the sensitizing fraction or product of the organism is one whose significance has not been appreciated or has yet to be discovered. Another disturbing factor is the widespread subclinical contacts with the ubiquitous streptococcus.

Finally, mention must be made of a possible virus etiology. Schlessinger et al.[94] found that deposits obtained by high speed centrifugation of pericardial fluid from cases of acute rheumatic pericarditis contain particles which morphologically resemble virus elementary bodies. Relatively pure suspensions of these bodies are specifically agglutinated by the sera of patients with acute rheumatic fever. These workers suggest that the bodies found in pericardial exudates represent the actual infecting agent. More recently[95] pericardial fluid from a patient who died of acute rheumatic fever has yielded a similar supposedly pathogenic agent. When injected intravenously into rabbits, scattered foci of inflammation in the myocardium and one or more valves were produced. These observations are preliminary and open a fertile field for intensive research.

Susceptibility of the Host. The host factor has been the outstanding disturbing factor in the experimental production of rheumatic-like lesions. There is no regularity in the degree and type of response to the various inciting agents. As yet, it is impossible to predict with any certainty the frequency or in which group of animals the lesions will develop. There exists in human beings an unquestionable predisposition to the production of antibodies.[97] Carlinfanti[86] notes that the predisposition for immunity is not a general nonspecific tendency to produce any type of antibody, nor even a property limited to only one antigen, but is a capacity referable to certain categories of antibodies. The relation between the tendency to immunity, which has been studied by biostatistical researches, and the allergic constitution has not been determined. Recent studies have revealed the association of unusually great antibody responses to diseases which are probably allergic in character.[87]

Genetic and epidemiologic studies[32] have established that susceptibility to rheumatic fever depends primarily upon the genetic

constitution of the individual and his chronological age. The distribution of cases in rheumatic families appears to follow the general laws of recessive mendelian inheritance.[44] A study of acute rheumatic fever in young adults, ages 18 to 42, disclosed that 21 per cent of the 266 patients gave a positive history for rheumatic fever in the parents or siblings.[37] At the present time, the susceptible child or adult cannot be identified. Coburn[52] estimates that about 5 per cent of human subjects in a mixed metropolitan population are constitutionally susceptible to the development of rheumatic fever. Biostatistical methods of analysis reveal that the most important factor in the pathogenesis of the disease to be susceptibility of the host.[31, 44]

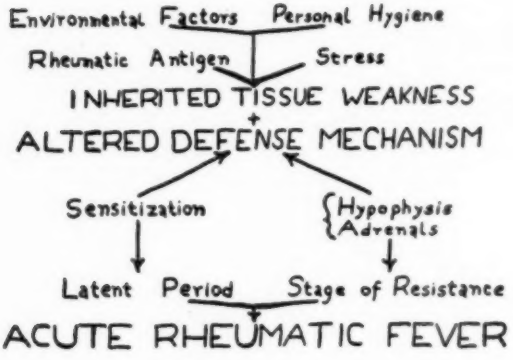
Relation of the Endocrine System. Various investigators have demonstrated antibodies in lymphocytes and the release of antibodies from lymphocytes.[20, 21] In mice, toxic agents fail to cause the liberation of antibodies from lymphocytes if the adrenals have been removed.[19] Such stimuli apparently cause the pituitary to produce excessive amounts of adrenocorticotropic hormones, which in turn induce the adrenal cortex to elaborate an excess of corticoids. The latter produce involution of the lymphatic organs and liberate antibodies from lymphoid tissue.[89]

Selye[8, 11] has suggested that the observations on the various changes of animals in response to many varied agents may be part of a general reaction of the body to a number of "alarming stimuli," which include different types of shock, exposure to heat or cold, infectious diseases, bacterial products, etc. The systemic manifestations incited by exposure to these stimuli are nonspecific and constitute a general "alarm reaction." This in turn is the first part of the "adaptation syndrome" and is followed by the "stage of resistance" and finally the "stage of exhaustion." The hormones of the anterior pituitary and the adrenal cortex exert considerable influence on the course and development of the adaptation syndrome.

Adaptation to our environment is a fundamental physiologic reaction in life and the capacity to adapt ourselves depends upon our genetic background. Desoxycorticosterone, when given to animals on a high sodium diet, produces myocardial and joint lesions similar to those observed in acute rheumatic fever.[11] Selye implies that it is not inconceivable, that while the defensive production of endogenous corticoids is useful in raising the resistance

of the body to stress, it would have certain detrimental side effects due to the inherent toxicity of the corticoids. This fundamental work[9, 11] suggests that such agents as bacteria, cold and immunological disturbances have so influenced the hypohyseo-adrenal

Diagram I



defense mechanism that an excess of corticoids are elaborated and that the rheumatic attack is the result of such a derailed defense mechanism.

CONCLUSION

The etiology of acute rheumatic fever has been discussed by medical scientists for more than 100 years and the riddle is still unsolved. However, our current etiological concepts form the basis for the so-called "prophylactic therapy"[65, 105] as it is known today. The vagueness of our ideas concerning this disease helps account for the many and diverse therapeutic regimes offered.[19, 21, 101, 22] Diagram I is an attempt to present in a graphic form a summary of the essential features of this paper. It is a suggestive diagram[92] and controversial in all aspects. After all, it is the thinking on this problem and the thinking on the problems of medicine that goes on in institutions of learning all over the world that in the end give us the principles of medicine, principles of understanding that have enabled man to inherit the earth and maintain and increase that inheritance.

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PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

INJURIES AND INFECTIONS OF NEWBORN CHILDREN*

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In the consideration of this subject we must first study

INFANT MORTALITY IN THE FIRST MONTH OF LIFE

The first four weeks may be regarded as the most dangerous period of human life; nearly one-tenth of the race succumbs in the first month of existence. As a result of scientific midwifery and strict asepsis, puerperal fever has practically disappeared; yet, as I shall be able to prove to you, the morbidity and mortality among young infants remains lamentably high. Beside the injuries of parturition and asphyxia the infant is far more susceptible to infections than the mother. Sudden death is very common, often due to unrecognized intracranial hemorrhage, atelectasis or pneumonia.

Eröss massed the vital statistics of sixteen large capitals of Europe, including 1,439,000 births. He found that 130,610, 9.5 of all children born, died in the first four weeks of life. In Budapesth, where the mortality in the first month is 8.11, he discovered that of these children 37 per cent died in the first week, 29 per cent in the second week, 21 per cent in the third week, and 13 per cent in the fourth week of life. The deaths in the earlier days were principally due to malformations, injuries of parturition and asphyxia. After the first week infections caused the majority of fatalities.

Axel-Johannessen states that the susceptibility to disease lessens with each month of life; the victims of congenital weakness,

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malformations, injuries of parturition die first and the survivors continually gain resistance to disease.

The following are Norwegian statistics. (Mortality by months of the first year of life.)

1st month	3.41 per cent	7th month	.52 per cent
2d "	.99 " "	8th "	.50 " "
3d "	.76 " "	9th "	.47 " "
4th "	.67 " "	10th "	.45 " "
5th "	.62 " "	11th "	.41 " "
6th "	.56 " "	12th "	.40 " "

9.80 per cent in the first year.

The same excessive death rate exists in Buffalo. During the year ending December 1, 1902, there were 7,290 births and 5,080 deaths. Of the deaths, 471 were in children under one month. Thus, 9.30 of all children born in Buffalo die in the first four weeks, and the death rate in the first months forms 6.4 per cent of the total mortality. Of these children

182—38.5 per cent—died in the first 24 hours
141—30.0 " " — " 2d-7th day of life
78—16.5 " " — " 2d week of life
34— 7.3 " " — " 3d " " "
36— 7.6 " " — " 4th " " "

It may be said that this is a normal mortality, that a large number of children are born who are incapable of living, but this position is erroneous. If we turn to the statistics of Norway (which has the lowest infant mortality in the world) we find that among 1,000,000 births in the rural districts from 1876-1898 the death rate in the first month is 3.38 per cent, about one-third of that of Buffalo. The records of a Norwegian country parish, Gloppen, have been carefully kept for 200 years. From 1687-1711 the mortality in the first month was 12.87 per cent; it has now fallen to 3.38 per cent, a diminution of about three-quarters. In the city of Prague the mortality in the first month is 14.2 per cent; in the Prague Hospital it is 3.3, showing conclusively that the life of the newly born child is most favorably influenced by good midwifery and nursing.

In contrasting the statistics of Buffalo with those of Eröss we

see that the mortality in the first month is 9.3 per cent, which is about the same as in the cities of continental Europe, 9.5 per cent; but in comparing the length of life, we notice that nearly double the number, 68.5 per cent, die in Buffalo in the first week, to 37 per cent in Europe. The number dying from the seventh to twenty-eighth day in Buffalo is 32.5 per cent, in Europe 63 per cent. We may, therefore, draw the conclusion that more children die with us from accidents of parturition and fewer from infections than in Europe.

As to the causes of death the malady or condition is often so vaguely described, that it is evident that a confusion of ideas exists. In Eröss' report, congenital debility is the most common term, claiming 80 per cent of deaths in the first month. It is, however, noteworthy that in Cologne in 1866-68, 5.20 per cent of all children born were recorded as dying of congenital debility, and in the next decade only 0.7 per cent were returned under the same title, indicating that the Cologne physicians had changed their phraseology.

Without doubt many infants are born before the full period of gestation, but they die of atelectasis, infections, meningeal hemorrhages. Absence of lesions does not indicate absence of microbes, which may be found in the fluids of apparently healthy tissues. A very large number of prematurely born underweight babies, reported as dying of immaturity, die of pulmonary or gastroenteric infections, or of cranial hemorrhage.

The mortality in early life is due to: (1) immaturity; (2) malformations incompatible with life; (3) asphyxia and atelectasis; (4) injuries of parturition and (5) various infections.

There were reported sixteen deaths from malformations, principally of the head and spine; nineteen deaths from congenital heart disease. This hardly seems creditable as patent foramen ovale and ductus arteriosus are compatible with prolonged existence. Cyanosis as a symptom of congenital heart disease is also seen in imperfect expansion of the lung and various infections.

From injuries of parturition, 21 deaths — 4.5 per cent
" convulsions - - 25 " — 5.3 " "
—
9.8 " "

The conditions of asphyxia and intracranial hemorrhage are most closely associated. The effect of prolonged difficult labor, abnormal presentations, not only favors the aspiration of foreign substances into the lungs and paralyzes the medullary respiratory centres with CO_2, but it also causes cerebral hemorrhages from traumatism, in the application of the forceps, by the nipping of a cerebral sinus in the forcible moulding of the head. Further, the intense cerebral congestion of dystocia may cause a rupture of the very fragile vessels of the pia mater. Hemorrhage is, in fact, the most frequent lesion found in infants stillborn, or dying soon after birth.

Dr. Herbert Spencer made a critical examination of 130 infants dying in the first few hours of life. In 65 per cent he found injuries to the brain, congestion and hemorrhages. He considers the forceps as the most frequent agent in producing hemorrhage. next, foot and breech presentations, softness of the skull and relaxation of sutures. He also discovered in many cases hemorrhages into the liver and suprarenal capsules, and pulmonary apoplexies. It is probable that a large number of children returned as dying of immaturity, insufficient vitality, asphyxia and convulsions succumbed to intracranial hemorrhage.

It must be remembered that while cerebral hemorrhage is usually associated with dystocia, it may occur in small children who are easily born. There may be no sign of cerebral irritation. The infant may die suddenly without symptoms, or may show irregular respiration and slight cyanosis, simulating asphyxia or atelectasis. Mistaking the condition for an imperfect expansion of the lungs, the physician may wonder why his well-directed efforts at resuscitation are unsuccessful. Generally, meningeal hemorrhage is the result of malpresentations and difficult labor. There is a series of convulsions, irregular breathing, cyanosis, opisthotonos, rigidity, quivering and automatic movements. The majority of cases die before the fourth day. The convulsions may subside and the child later suffer from epilepsy or paralysis. The slight hemorrhage may give rise to no immediate symptoms. Many cases of idiocy, dull mentality, epilepsy, hemiplegia and diplegia, trace their origin to intracranial injuries of parturition.

The diagnosis of meningeal hemorrhage or internal hematoma of the meninges may be made with great accuracy, with the his-

tory of an external hematoma, difficult labor and recurring convulsions. The treatment of intracranial hemorrhage is almost hopeless; even if the convulsions are relieved, the residual disabilities are not lessened.

CASES ILLUSTRATING CLINICAL HISTORY OF MENINGEAL HEMORRHAGES

The following is the history of a case that I think would be diagnosed as *feeble vitality, congenital debility or heart disease.* Baby born after a normal labor lasting two hours, head presentation, died aged six hours, growing blue in the face, no convulsions.

Autopsy. Plump baby, thymus large, lungs expanded, ecchymoses in the pleuræ; stomach and intestines contain large quantities of viscid mucus; a film of blood over motor areas of cortex, large clot at base of brain about cerebellum and medulla, small clot in ventricles. Here the hemorrhage was due to the moulding of the head in an easy labor.

Meningeal Hemorrhage Causing Convulsions. Called at 9 P.M. to see a child born sixty-three hours before; mother primipara, twin birth, the fetus undeveloped 3/12 gestation, 2 placentas, 1 shrivelled small; 1 normal. Second stage lasted seventeen hours, presentation right occipito-posterior; instruments used; easy delivery; cord tight about neck. Child slightly asphyxiated; an extensive edemata of neck, present for thirty-six hours; a hematoma size of hen's egg on left occipital bone, slight forceps abrasion on left trapezius; defecation and urination normal, umbilicus normal; heart sounds good, strong; respirations called for. Languor, cyanosis and convulsions. First convulsion when fifty hours old, after feeding, one in late morning, one in afternoon, 8:30 P.M., a series of hard convulsions; rigidity and twitching of extremities, some of the convulsions were caused by swallowing, showing exaggerated pharyngeal reflex. Child blue and feeble; evening temperature 103°F.; advised cold to the head and chloral. The child had no more convulsions and died at 11:30 P.M.

Next is the history of a case, with *long continued convulsions, partial recovery, development of epilepsy, death in status epilepticus.* Called to see child seventeenth day of life for frequent convulsions. History: born after normal labor, easy head pres-

entation, non-instrumental; second day of life child began to have convulsions, would become cyanotic, breathe rapidly, and have twitching of extremities. In the intervals of relaxation baby apathetic and would not nurse; fed breast milk. Defecation in order; temperature in axilla for last ten days 102° F. Child had grown weaker and thinner, five to fifteen convulsions a day, generally in afternoon and night. Examination on the seventeenth day: child very thin; temperature 97.6° F.; respiration 50; heart sounds weak, 120; right parietal large hematoma; child grew cyanotic when handled; umbilicus unexcoriated; passed a foul mucous stool. Later history: the convulsive attacks gradually grew less frequent; in later infancy ceased for a month; then recurred at frequent intervals; child was fat with a type of flaccid palsy; blind from optic atrophy; child died aged two years in status epilepticus.

I wish also to report a *case of difficult delivery, child born asphyxiated, completely resuscitated; there were no convulsions; no rigidity or loss of power.* This child throve, and, until it was eighteen months old, there was no evidence of intracranial injury. At this age it was noticed that the child moved awkwardly and could not walk; signs of spastic paralysis developed, and now, at the age of four years, the patient is the victim of spastic diplegia, Little's disease. There are exaaggerated reflexes, stiffness and incoordination in the upper and lower extremities, strabismus and dull mentality. The cause of the child's disability was a meningeal hemorrhage of the cortex, over both motor areas, with secondary degeneration of the anterior and lateral pyramidal tracts of the spinal cord.

ASPHYXIA AND ATELECTASIS PULMONUM

Seventeen deaths were recorded from asphyxia, atelectasis and compression of the cord, 3.6 per cent of total mortality. Asphyxia and cerebral hemorrhages are usually caused by the same conditions of dystocia and have in common the symptoms of prostration, cyanosis and irregular breathing. Asphyxia is ordinarily completely relieved by artificial respiration, but a number of cases are seen where treatment is only able to effect a partial expansion of the lungs; the infant lives for days and weeks with one-third to one-fourth of its lungs in working order. It is feeble, has a

subnormal temperature, will not cry or nurse, breathes rapidly, irregularly; suffers from frequent cyanotic attacks, in one of which it may die.

In congenital atelectasis there may be an easy labor, no asphyxia, but from inherent weakness or immaturity of the respiratory muscles and nerve centres the baby will not expand its lungs. It leads a cold, cyanotic vegetative existence; refuses food and is apt to die suddenly in an attack of cyanosis. In both asphyxiated infants and those suffering from atelectasis there is feeble or absent breath-sounds at the bases of the lungs; underweight children, or those born asphyxiated, should be occasionally ausculated and closely watched. With lividity, rapid or irregular breathing, oxygen, mustard baths, artificial respiration, forced feeding and hypodermic stimulation should be used with vigilance. A large number of these cases may be saved.

Both asphyxia and atelectasis are fertile causes of bronchopneumonia.

SEPSIS

A large proportion of fatalities in newborn infants are from sepsis. The avenues of infection are numerous, and include the eye, ear, nose, mouth, skin, digestive and respiratory tracts and umbilicus. The germ may be any one of the pathogenic bacteria. The patient's resistance to disease is very slight, probably owing to deficient leukocytosis and defective development of the lymphatic apparatus. When puerperal fever prevailed young infants were frequently infected by their mother's milk. In Prague, after the introduction of antiseptic methods in the hospital, the mortality of the newly born sunk from 30 per cent to 5 per cent, and the number of feverish children from 45 per cent to 11.3 per cent. Indeed, the conditions are often more favorable for infant life in a fine hospital than in an ordinary dwelling. According to Birsh-Hirschfeld, prenatal infection, save for lues, is almost impossible. The healthy placenta is a perfect filter for germs. It is only when the placenta is diseased or saturated with bacteria that infection is possible. It is favored by partial detachment of the placenta or frequent hemorrhages. The greatest source of danger is the amniotic fluid after the bag of waters is prematurely broken. The amniotic fluid is polluted by the examining finger

or by an ascending infection. The fluid is aspirated into the lungs or swallowed and infection may become general or localized, in the respiratory or gastro-enteric tract. The germ is generally the colon bacillus. A period of incubation may occur, and several hours or a day or two may elapse before symtoms appear.

Whatever be the microbe or portal of invasion, the infection soon becomes general, and nearly every autopsy will reveal a pneumonia. To discuss the matter in detail would be to allude to symptoms arising from lesions of every organ. The general clinical picture is fever, cyanosis, rapid breathing, convulsions, vomiting and diarrhea. (Mother usually well, free from fever.) It must be remembered that in a prematurely born child, weighing from 1,500 to 2,000 grams, a virulent infection may exist without a rise in temperature. Most cases of sudden death may be explained in this way; there is no ability to defend the organism against toxins.

It is usually stated that the umbilicus is the vulnerable point. I doubt if many infant deaths are due to this cause. Three deaths of 471 are returned from lesions of the navel at the fourth, nineteenth and twenty-second day; it is possible the condition is more frequent owing to the fact that physicians are slow to acknowledge that a preventable disease has occurred in their practice.

Respiratory inflammations are excessively common in the first month. The disease may start from purulent coryza, an imperfectly expanded lung or a pulmonary apoplexy. The infection may come from foul atmosphere, unclean bedding or mattress, as seen in the Heidelburg epidemic, where an epidemic of 8 cases arose from staphylococci in straw beds, but it is more frequently caused during parturition, by the aspiration of amniotic fluid, contaminated by the colon bacillus, streptococcus or staphylococcus. The number of deaths reported, 40, 8.5 per cent, does not accurately state the frequency of the disease, as a majority of infants dying in the first month have a bronchopneumonia. Pneumonia is diagnosed principally by objective signs, fever, cyanosis and rapid breathing. There are no characteristic physical signs in the chest and the treatment is hydrotherapy, counter irritation and stimulation. Delestre states that the majoriy of autopsies in prematurely born children show a hemorrhagic bronchopneumonia, causing almost an absolute obstruction in the bronchial tubes.

Richter, of Vienna, made 1,525 autopsies upon children dying suddenly in the first month. He found the most frequent cause of death was a capillary bronchitis, which killed by asphyxia. The bronchitis was occasionally associated with bronchopneumonia or intestinal catarrh. As to other causes of sudden death, Epstein said the diagnosis of hypertrophy of the thymus was a term used to mask our ignorance of the real cause of death.

GASTRO-ENTERIC INFECTIONS AT BIRTH

Gastro-enteric infections at birth are occasionally seen and receive small mention in textbooks. In Buffalo, in the year ending December 1, 1902, there were among infants under one month, thirty deaths from acute gastro-enteric disease, and forty from marasmus and inanition, making 16 per cent of the total mortality under four weeks.

With some children a congenitally imperfect digestion exists, the digestive ferments are weak, the congested gastro-enteric tract is coated with mucus, and autointoxication or infection readily occur. Vomiting, diarrhea and colic are easily excited, and may be due to mere dyspepsia, to grave gastro-intestinal infection or autointoxication, or to general sepsis. Delestre describes a chronic infection causing infantile atrophy or athrepsia. Dyspepsia may be caused by colostrum, breast milk, or by injudicious food mixtures.

Severe gastro-enteric infection is in my experience more frequent and fatal in newborn babies than lesions of the umbilical wound or vessels. The germ may enter the digestive tract in various ways, on the accoucheur's or nurse's finger in the toilet of the mouth, by breast milk or food-prescription. It may be sucked from the breasts of the mother or may be introduced by the swallowing of polluted amniotic fluid or vaginal secretion during the infant's sojourn in the parturient canal. Amniotic fluid is often present in the stomach of the newborn babies, and is, of course, not always pathogenic. Karlinski discovered pus cocci in the milk of a sick mother and in the food and intestinal contents of her baby, dead of septicemia. Before the days of asceptic midwifery, a close association was observed between infantile diarrhea and child-bed fever. The mother was infected during or after parturition and the baby swallowed bacteria in the breast milk. Now-

adays, the mother remains well, while between 9 per cent and 10 per cent of all children born die in their first month of life.

Between dyspepsia and gastro-enteric sepsis, the dividing line is vague, often depending on the dose and virulence of the poison and the resistance of the individual. Microbes, habitually inoffensive, may become virutently pathogenic.

In Grosz's statistics of the morbundity of young infants, of 447 newly born hospital children, 254, or 57 per cent, showed food vomiting or dyspeptic diarrhea. He says the rapidly fatal choleriform diarrheas, formerly seen, now seldom occur.

Grosz's diagnosis of dyspepsia was based on an illness of ten days with vomiting and frequent mucous stools. He describes three grades of dyspepsia: (1) Several yellowish green stools daily; (2) same symptoms with vomiting; (3) stools dark green color, frequent vomiting and a rapid loss in weight.

The five cases of diarrheal disease in newborn children which I report are of a much graver character than Grosz's subdivisions of dyspepsia. They are best described as gastro-intestinal sepsis or ileocolitis. The babies were of good weight and sound, vigorous physique. They were evidently poisoned during or soon after birth by some virulent germ which, besides exciting acute gastro-enteric irritation, profoundly depressed the respiratory and cardiac centres. The three survivors showed no signs of digestive or constitutional weakness in later infancy. As soon as the poison had been eliminated or had lost its virulency the children throve with their mother's milk.

First Case. This is possibly one of *severe dyspeptic diarrhea,* yet the baby was failing so rapidly in the hot month of August that the illness was diagnosed as an ileocolitis. The confinement was normal and the umbilical wound healed quickly. The mother had plenty of milk and attempted to nurse her baby boy; a diarrhea quickly ensued with six to eight green mucous stools a day. Temperature, 100°-103° F. The breast milk was analyzed and proved to be a colostrum milk, highly albuminous. In spite of treatment and a change in diet to cereal gruels and whey the diarrhea continued and increased in severity for twelve days. At the fourteenth day of life the frequency of the stools, the child's prostration and emaciation (one-fifth of the weight, twenty ounces, had been lost) made the patient's condition somewhat alarming.

A wet-nurse was procured with a gradual amelioration of all symptoms. Later, the mother nursed her child, and at the age of four months it weighed twenty pounds.

Second Case. The patient was the third child, born October 15; two other children died shortly after birth. The baby was born with the cord about the neck; the baby was partly asphysiated and well resusciated. Immediately after its birth the child seemed feverish, apathetic, and would not nurse its mother or a wet-nurse. For the next three days the baby appeared very ill; October 16, the temperature was 104° F.; on October 17 it was 102° F.; on October 18, 102° F. It refused the breast, was fed on diluted breast milk, and had two to three foul, mucous stools daily. I first saw the case October 19, the fifth day of life; the baby was large, well developed, but languid and exhausted. Temperature, 100° F.; pulse, 140. I removed the cord; the umbilical wound was healthy. There was a livid erythema of the mouth and numerous stools of mucus and food débris.

October 20, same condition of prostration and diarrhea.

October 21, the patient grew rapidly worse; temperature 101.5° F.; respirations 84; pulse 140. Persistent vomiting of food and bloody mucus, frequent stools of mucus and blood; the baby was almost continually rigid, with opisthotonos and carpopedal spasms.

October 22-23, the same symptoms of tonic spasms of the trunk and extremities with frequent vomiting and stools of bloody mucus.

October 24, the child died at 9:30 A.M.

Autopsy. The body was much discolored; the lungs were congested at the bases; the right ventricle was distended, esophagus congested; stomach dilated and congested; entire intestinal tract congested and coated with bloody mucus; umbilical vessels healthy; brain not examined.

The duration of the malady was ten days; the patient seemed ill from the moment of birth. In its sojourn (asphyxiated condition) in the parturient canal the baby in efforts at breathing may have swallowed polluted amniotic fluid or vaginal secretion, producing a fatal gastro-enteric infection. The nervous symptoms, opisthotonos and carpopedal spasms were probably the result of general sepsis.

Third Case. Baby born October 8, 1901. Normal labor, no

asphyxia, weight about eight pounds; child nursed on the second day; the breast milk was noticed to be unusually thick and creamy. The baby throve until the fourth day of life; then grew somnolent and would not nurse; the stools became frequent, seven to eight daily, were black, foul-smelling and contained strings of mucus. I saw the patient the sixth day of life. The baby looked very badly, temperature 102° F.; heart, weak and rapid; umbilicus, healthy; fragment of mummified cord sprinkled with boric acid was hanging to the navel.

From October 14-19, the symptoms were numerous, fetid, mucous stools, fever and increasing prostration. The baby was sparingly fed on diluted breast milk, whey and gruels. It was given calomel, intestinal irrigations, strychnia, whiskey and artificial serum.

October 20, the patient grew rapidly worse; the rapid breathing suggested a pneumonia; the diarrhea continued with frequent attacks of cyanosis. Death occurred October 21. No autopsy was permitted. The illness lasted ten days. The gastro-enteritic tract was probably infected through the breast milk, which was thick and slimy.

Fourth Case. The mother was a primipara of thirty. The labor was long and difficult, lasting fifty-seven hours on account of rigidity of the cervix. Opium and hyoscyamus was given in the earlier stages of parturition. Head presentation, delivery was effected by forceps under chloroform narcosis. The accoucheur introduced his fingers into the rectum to assist delivery, rinsed them off in sublimate solution, and wiped out the baby's mouth with sterile gauze. The child weighed eight and three-quarter pounds, was at once put to the breast, although the secretion of milk was not established until the fifth day. When twenty-four hours old the baby began to vomit and pass black liquid stools, containing mucus and blood.

April 10: I first saw the child on the third day of life; it looked very ill, had cried for hours in a hoarse, gasping way; there was no cyanosis; temperature 103° F., heart so rapid and feeble that the child seemed moribund. With stimulation and intestinal irrigation the child revived somewhat, yet for four days it was very feeble and required heroic doses of whiskey, strychnia and hypodermoclysis. The temperature ranged from 102°-106° F.;

respiration 50-60. There was occasional vomiting and numerous stools, ten to twelve daily, of bloody mucus and food debris; the food was diluted breast milk from a wet-nurse.

After April 13 the baby slowly improved, and the fever gradually subsided. The acute symptoms lasted for six days. Prostration and imperfect digestion continued for three weeks. The mother nursed the child when two weeks old; the baby is now in superb condition.

Infection in this case may have occurred from swallowing amniotic fluid, or more probably from the toilet of the mouth through the finger of the accoucheur which had previously been introduced into the mother's rectum.

Fifth Case. The mother a primipara of thirty-three. Labor easy, noninstrumental. Baby born September 26; weight seven and one-half pounds; the baby was put to the breast and had normal meconium stools for two days. The third day the child showed fever 102° F.; the respirations became rapid and irregular, 80; a serious diarrhea appeared, 12 stools containing blood and mucus in twenty-four hours. I saw the child at 5 P.M.; it had been stimulated with strychnia and atropia. Temperature, 99.5° F., pulse, 120; color, good. The malady had strangely affected the rhythm of respiration. The breathing was rapid, irregular and superficial, only an occasional inspiration would inflate the lower lobes; umbilicus, healthy. On the fourth day the temperature at 2:30 A.M. was 101° F.; there were twelve bloody, mucous stools in twenty-four hours; at 9 A.M., the child sank into desperate collapse with marked respiratory failure; after two hours' work with oxygen and hypodermic stimulation, the child improved and at noon was in fairly good condition.

During the next three days, October 1, 2 and 3, there was no fever; the respiration was irregular and superficial; there were five to eight black, bloody, mucous stools a day. The baby was so weak that it was fed with a medicine dropper.

On October 4, the mother began to nurse the baby; the respiration gradually grew deeper and more regular. Mucus and undigested food debris were present in the stools for two weeks; the loss in weight during the first week amounted to only twelve ounces. The baby is six months old, now in good health. The cause of the infection was impossible to discover.

This little series of cases of diarrheal disease in newborn children was seen in consultation practice, among well-to-do families, with good hygienic surroundings. The mode of infection is obscure, but I have a most positive impression that in two cases (1 and 3) the mother's milk was the cause of illness and that in one case (2) the child was infected in the parturient canal, probably by swallowing amniotic fluid containing the colon bacillus. All of the mothers attempted to nurse their children, and no other food than breast milk was given until fever, vomiting and diarrhea appeared. Colostrum or infected breast milk may excite a severe or fatal diarrhea. If the mother's milk be suspected, nursing should be stopped at once. It should be remembered that while colostrum milk may temporarily be very irritating, that the excess of albuminoid is apt to disappear in a few days, when nursing may be resumed.

The prevention of gastro-enteric disease in the newborn is effected by vigorous asepsis, and especially by avoiding unnecessary toilet of the mouth with unsterilized fingers or gauze, as these infants are very prone to infections of the lungs and digestive tracts.

If the physician wishes to succeed in saving a newborn child who shows signs of grave infection, he must keep it under close personal observation. At this early age attacks of sudden cardiac and respiratory failure are frequent and unexpected, and require prompt hypodermic stimulation with strychnia, atropia and normal salt solution. For food, diluted breast milk should be given. Other adjuvants of treatment are hydrotherapy, laxatives and gastric and intestinal lavage.

The diseases of the newborn are little studied or understood. The high mortality of the first month could be much lessened if the unnecessary use of the forceps were avoided and surgical cleanliness were observed about the child as well as the mother.

CLINICAL-PATHOLOGICAL CONFERENCE

WILLARD PARKER HOSPITAL, NEW YORK

Meeting held April 19, 1949

DR. APPLEBAUM, presiding.

TUBERCULOUS MENINGITIS

DR. SILVERBERG presented Case No. 4163, a 21-month-old negro female, who was admitted to Willard Parker Hospital on June 26, 1948 and expired about eight months later, on March 4, 1949 of tuberculous meningitis.

This infant was transferred from another hospital with varicella, and as an exposure to measles. She was hospitalized in that hospital from May 28, 1948 until her transfer here, and was being studied there for persistent non-productive cough and intermittant fever. A chest x-ray taken there revealed a pneumonic density in the right upper lobe. Her tuberculin (1:10,000) was negative and the lesion did not respond to therapy.

On Admission to Willard Parker Hospital, this patient had a typical case of varicella, which subsided uneventfully. However, she was noted to have a slightly productive cough, and coarse rhonchi scattered throughout her right chest. A routine chest plate taken on June 29, 1948 revealed a massive consolidation of the right upper lobe, and small miliary nodules scattered throughout both lungs. A tuberculin (1:10,000), done a few days after admission here, was strongly positive. The neurological examination and the remainder of the physical examination were essentially negative.

Hospital Course. During the first week and a half here, the patient spiked a daily temperature of 102° and 103° F. Except for occasional rhonchi in the right chest, her physical examination during these temperature spikes was negative. However, on the ninth hospital day, she began to show transient neurological signs: spasm of her hamstrings, she would not stand when placed on her feet, and there was some slight ankle clonus. These signs, together with the chest x-ray, suggested the possibility of an early tuberculous meningitis. Several spinal taps revealed normal sugars, Pandy 72+, and increase in cells, mainly monos. In spite of the normal sugar, it was thought best to start intramuscular

streptomycin, 1 gram daily for possible tuberculous meningitis, and possible miliary tuberculosis. It was not until nearly one month later, August 4, 1948, the spinal fluid sugar fell to 22 mg.%, thus making the diagnosis more certain. At this time, promizole and intrathecal streptomycin were added to the therapy (after she had received 50 injections intrathecally, this was temporarily distinued because of local arachnoiditis).

By November 1, 1948 the patient seemed to be doing extremely well. She was alert and playful, and all evidence of abnormal neurological signs was absent. Her spinal fluid sugar rose to 50 mg.%. At this time streptomycin was discontinued, and patient was only receiving promizole. She continued to do well for about a month, and then began to spike daily temperatures again. A relapse was suspected and streptomycin was again instituted. By December 16, 1948 her spinal fluid was down to 10 mg.%, and neurological signs were present—nuchal rigidity, positive Kernig and Brudzinski. Patient was apathetic and could not take oral feedings.

On January 1, 1949 a spinal fluid culture was reported positive for tubercle bacilli, and the intrathecal streptomycin dose was increased.

In spite of therapy, her course was steadily downhill. She became increasingly spastic and comatose. During the last month, her position in bed was that of marked opisthotonos. During this time she was fed by gavage.

During the last two or three weeks, marked ulceration of the skin at pressure points was noted. She had several convulsive seizures and numerous episodes of Cheyne-Stokes respiration. The patient expired on March 4, 1949.

Autopsy Findings by Dr. Dolgopol. The body was that of a poorly nourished negro female child. There was an area of impetigo on the head. The circumference of the skull was 46 centimeters, which was within the normal limits for a child 27 months old. However, there was some diastasis of the cranial sutures measuring 4mm. in width. The very thin skull was opened along the sutures by means of scissors and the parietal and occipital bones were reflected for the purpose of removing the brain. On removing the brain about ten ounces of blood-tinged fluid escaped from the ventricles as the thin left hemisphere tore in the process of removal. After the loss of fluid, the brain weighed 740 grams,

showing a marked loss of the brain substance. The normal weight for the age would be about 1100 grams. The cerebral hemispheres collapsed after the escape of the fluid, and the left was particularly thin. The base was covered with spongy grayish exudate and showed numerous adhesions in the fissures. The choroid plexuses were thick and covered with gray exudate. Thin bands of fibrin stretched from one wall to another in the distended left ventricle. All ventricles were lined with a soft grayish membrane. Some fibrin was present in the aqueduct. The roof of the fourth ventricle and the base of the cerebellum were matted together by spongy gray exudate. The fourth ventricle was markedly dilated. An irregular white area surrounded by a zone of softening was present in the left basal ganglia and microscopically proved to be a tuberculoma. Several areas of cortical softening were present in various parts of the brain. A few small tubercles were present in the meninges over the hemispheres. A portion of spinal cord was removed and showed a marked thickening and edema of the meninges. The upper lobe of the right lung contained a yellowish round pedunculated structure, situated on the wall of the smooth cavity which apparently was connected with a bronchus. Smears from that area contained acid-fast bacilli, and a guinea pig inoculated with that material developed tuberculous lesions. All lobes of both lungs showed areas of lobular consolidation which did not appear tuberculous in character. There were no enlarged lymph nodes in the hilar regions. No tubercles were seen grossly in the liver, spleen and kidneys.

Microscopic sections of the various organs were shown: The caseous area in the left basal ganglia consisted of caseous necrotic tissue with some dust-like deposit of calcium. Some of the blood vessels of the meninges surrounded by tubercules showed marked thickening of their intima. This explains the numerous areas of cortical softening. The ependyma of the ventricles was replaced by tuberculous granulation tissue. The tuberculous process involved the floor and the lateral walls of the fourth ventricle, including the areas of the vestibular nuclei.

A tuberculous process involved the meninges of the spinal cord. A small recent tubercle and an old scarred tubercle were found in the liver. The heart, kidneys and spleen showed no tuberculous involvement.

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